**NEW DRUGS**

**Extended-Release Carbamazepine For Bipolar Disorder**

The U.S. Food and Drug Administration (FDA) has approved extended-release carbamazepine capsules (Eqeetro™, Shire), formerly called SPD417, for patients with acute manic and mixed episodes associated with bipolar I disorder. The drug was approved 10 months after the company’s application was submitted to the FDA.

Bipolar disorder, also known as manic depression, is one of the six leading mental disorders worldwide, according to the World Health Organization. Each year, more than two million American adults (about 1% of the population aged 18 and older) are affected. The disorder is characterized by episodes of mania and depression, with periods of normal mood in between.

In clinical trials, Eqeetro™ significantly reduced manic symptoms in bipolar patients. It had a favorable side-effect profile, and no clinically significant weight gain or increase in blood glucose levels was observed. By the end of the trials, patients experienced improved scores on several rating scales.

The product comes in 100-, 200-, and 300-mg dosage strengths and will be available in the U.S. in early 2005.

(Source: 17th annual U.S. Psychiatric and Mental Health Congress, San Diego, November 18, 2004; Shire.)

**Eszoplicone for Long-Term Treatment of Insomnia**

Sepracor, Inc., has announced the FDA’s approval of its New Drug Application (NDA) for the sleep aid eszopiclone (Lunesta™, formerly Estorra™).

The recommended dosage for improving sleep onset or maintenance is 2 or 3 mg for adults and 2 mg for adults 65 years of age and older). The 1-mg dose is indicated for sleep onset in older adults whose primary complaint is difficulty falling asleep.

Data from a landmark, six-month, double-blind, placebo-controlled safety and efficacy study in 788 patients were reviewed by the FDA as part of the NDA submission for eszopiclone and served as a basis for the agency’s decision to not limit the drug’s indication to short-term use. Sepracor’s study was the first of its kind for a prescription non-benzodiazepine for insomnia.

The company plans to evaluate eszopiclone in patients with depression or pain and in women who are experiencing the effects of perimenopause.

Patients should take this drug only when they are prepared to get a full night of sleep.

(Source: Sepracor, December 16, 2004.)

**Palifermin Reduces Mucositis From Cancer Treatments**

Amgen’s new intravenous biological product, palifermin (Kepivance™), has been approved to help reduce the development and duration of mucositis in patients with leukemia and lymphoma who are undergoing chemotherapy and radiation in preparation for bone marrow transplants.

Mucositis, which consists of painful sores and ulcers in the lining of the mouth, is a common complication of the high-dose chemotherapy and radiation therapy regimens associated with bone marrow transplantation. Patients have difficulty eating and swallowing. In the most severe form of mucositis, patients cannot eat or drink at all and must receive nutrition and fluid replacement through the veins.

Palifermin is a synthetic version of a naturally occurring human protein called keratinocyte growth factor (KGF). KGF stimulates the growth of cells in the skin and on the surface layer of the mouth, stomach, and colon. Like natural KGF, palifermin also stimulates cells on the surface layer of the mouth to grow. This is thought to lead to faster replacement of these cells when they are killed by cancer treatments and to speed up the healing process of mouth ulcers.

In a study of 212 patients with leukemia or lymphoma who were receiving high doses of chemotherapy and radiation treatments associated with bone marrow transplantation, severe mucositis developed in 63% of patients receiving palifermin, lasting for an average of three days, and in 98% of the placebo patients, lasting for an average of nine days.

(Source: Amgen, December 15, 2004.)

**Generic Zoloft®**

Ivax Corporation has received tentative approval from the FDA for its Abbreviated New Drug Application (ANDA) for sertraline HCl tablets in 25-, 50-, and 100-mg dosage strengths.

Sertraline HCl is the generic equivalent of Pfizer’s Zoloft®. Ivax believes that it has first-to-file status on this drug and that it will be entitled to 180 days of marketing exclusivity.

In 2002, Pfizer settled its infringement lawsuit with Ivax. Ivax plans to launch this product in June 2006.

(Source: Ivax, December 9, 2004.)

**Hyaluronate for Osteoarthritis of the Knee**

The FDA has granted a Premarket Approval Application (PMA) for 1% sodium hyaluronate (Nuflexxa™, Savient Pharmaceuticals, Inc.).

Nuflexxa™ is indicated for the treatment of pain in osteoarthritis of the knee in patients who have not responded adequately to conservative nonpharmacological therapy or simple analgesics. The product has been approved in Europe as Euflexxa™.

This is the only non-avian–derived
hyaluronic acid approved in the U.S. It is a product of Bio-Technology General (Israel) Ltd., a Savient subsidiary. (Source: Savient, December 7, 2004.)

**DRUG NEWS**

**Aromatase Inhibitor Better Than Tamoxifen in Preventing Breast Cancer Recurrence?**

A newer drug may be superior to tried-and-true tamoxifen (Novaldex®, AstraZeneca) at preventing breast cancer from recurring. Anastrozole (Arimidex®, AstraZeneca) prevented far more breast cancers from recurring in older women than tamoxifen and caused fewer side effects. Doctors say that the new drug might be able to prevent up to 80% of the most common tumors that occur in women after menopause, compared with the 50% rate attributed to tamoxifen.

Currently, women with breast cancer that is responsive to hormonal treatment as well as postmenopausal patients are advised to take tamoxifen for five years. However, tamoxifen causes side effects, including endometrial cancer and blood-clotting disorders, and there is still a chance of spread or return.

Cancer specialists said that anastrozole is likely to become the first-choice treatment for most women who have had the disease, and they predicted a wider role for similar drugs of its type, the aromatase inhibitors. Some experts, however, say that it is too early to tell whether using aromatase inhibitors from the outset will be better than using tamoxifen first, followed by the newer drugs.

Anastrozole blocks the body’s manufacture of estrogen, a hormone that promotes the growth of most tumors that occur in postmenopausal women. Tamoxifen blunts estrogen’s effects.

Drugs like anastrozole inhibit aromatase, an enzyme used by bodily tissue to make estrogen, but they do not stop the ovaries from making estrogen. Aromatase inhibitors are prescribed for patients past menopause, after their ovaries stop making estrogen, but the drugs may not work in younger women.

For women with early-stage breast cancer who took anastrozole for five years, cancer was less likely to recur, to develop in the other breast, or to spread, compared with tamoxifen.

Some experts, while agreeing that the new findings were encouraging, called the authors’ conclusions premature; other research suggests that women might gain a slight advantage by taking the two drugs sequentially (i.e., tamoxifen for two to three years, followed by an aromatase inhibitor). It will be at least another year before researchers will be able to directly compare an aromatase inhibitor alone with a combination of the two drugs.

The study, funded by AstraZeneca, involved nearly 2,000 American women and an additional 7,300 women from 20 other countries for roughly five years.

Because the women in the new study had early cancers and were observed for only five years, there was no difference in survival rates. The women who took anastrozole reduced the chances of their cancer spreading by 14% and were 42% less likely than women taking tamoxifen to develop a tumor in the other breast. They also suffered fewer side effects.

Other aromatase inhibitors include letrozole (Femara®, Novartis) and exemastane (Aromasin®, Pfizer).

(Source: *The Lancet* online; Associated Press, December 8, 2004; *The New York Times*, December 9, 2004.)

**More Approvals for Injectable Pantoprazole**

Wyeth has received the FDA’s Supplemental New Drug Application (SNDA) approval for room-temperature shipping and storage of pantoprazole sodium for injection (Protonix® IV). This was the first proton-pump inhibitor (PPI) in the U.S. to be offered in both oral and intravenous (IV) formulations.

As a result of this approval, IV pantoprazole can be stored at room temperature after it is shipped to customers. Room-temperature storage represents a substantial improvement in stocking the product in hospital pharmacies and patient-care areas.

The FDA first approved this product in March 2001 for the short-term treatment of patients with gastroesophageal reflux disease and a history of erosive esophagitis as an alternative to oral therapy in patients who were unable to continue taking Protonix® delayed-release tablets. (Source: Wyeth, November 15, 2004.)

**Rivastigmine May Help Parkinson’s Disease Patients with Dementia**

A medication used to treat Alzheimer’s disease (AD), rivastigmine tartrate (Exelon®, Novartis), provides important benefits in symptoms of dementia in patients with Parkinson’s disease (PD). Patients who took rivastigmine functioned better overall and showed improved cognition and behavioral symptoms, compared with patients taking placebo.

A chronic and progressive disease of the nervous system, PD affects 1.5 million Americans. Rivastigmine, which has been approved for patients with mild-to-moderate AD, has demonstrated statistically significant benefits in a large-scale, well-controlled study.

Dementia affects approximately 40% of patients with PD and may affect up to 80% of them as the disease progresses.

Previous studies suggest that patients with PD have up to a six-fold increased risk of developing dementia compared with elderly patients without PD. More patients taking rivastigmine improved in the 10-item Neuropsychiatric Inventory...
and in tests for memory, attention, the ability to carry out daily activities, planning, and reaction times compared with patients taking placebo.

More patients reported increased tremor with rivastigmine than with placebo, but this rarely resulted in withdrawal from the study.

The weight loss associated with rivastigmine occurred more commonly among women receiving high doses in clinical studies.

People at risk for some heart conditions or stomach ulcers should notify their doctors before taking rivastigmine.

(Sources: N Engl J Med, December 9, 2004; www.exelon.com.)

**Warnings of Amiodarone**

**Risks for Heart Patients**

After a delay of more than a year, the FDA has approved the publication of new warnings for a potentially risky heart drug taken by millions of Americans.

Patients taking amiodarone (Cordarone®, Wyeth) were expected to be able to read the new warnings on the Internet beginning in mid-December. They will receive paper copies when they fill or refill prescriptions. The FDA has recently been under fire for failing to protect consumers from dangerous drugs.

It is not known why the guide, planned since October 2003, was delayed. As of this writing, the guide was undergoing final editing and Wyeth was working on getting printed copies of the guides to pharmacists. Patients will be able to view the final version at www.wyeth.com.

Amiodarone has been associated with numerous side effects, including lung toxicity, thyroid problems, and liver damage. Because of its dangers, amiodarone was approved only as a drug of last resort for specific life-threatening ventricular arrhythmias. Over time, however, it gained favor with cardiologists for the treatment of atrial fibrillation, a less serious heart rhythm condition.

Physicians wrote more than two million prescriptions in a single year for atrial fibrillation and other heart conditions that amiodarone was not approved to treat. For the year ending July 31, 2003, 82% of the drug’s retail sales were for unapproved uses, according to a Knight Ridder analysis.

Although many cardiologists defend amiodarone’s “off-label” use for atrial fibrillation, a National Institutes of Health study challenged their long-held beliefs. The study found that less risky drugs could be as effective as amiodarone.

(Sources: www.myrtlebeachonline.com; Philadelphia Inquirer, December 8, 2004.)

**Celecoxib: New Heart Risks**

Pfizer has announced that it found an increased risk of heart problems in some people taking higher dosages of celecoxib (Celebrex®), its popular arthritis and pain relief drug. The findings came three months after Merck withdrew rofecoxib (Vioxx®), a chief competing COX-2 inhibitor. One of two long-term studies had found that rofecoxib doubled the risk of heart attack and stroke.

Pfizer did not have immediate plans to pull celecoxib from the market, but it did plan to pull television advertisements. Its shares slid on the news of the study, then rebounded. The company’s Web site reported $1.9 billion in revenue from celecoxib sales in 2003.

In October 2004, the first month after rofecoxib’s withdrawal, an estimated 2.3 million prescriptions were written for celecoxib, up from 2 million in September. That has ebbed somewhat, but celecoxib still accounts for about 11% of all new prescriptions written by primary care physicians.

Patients taking celecoxib should discuss appropriate treatment options with their physicians.

Pfizer emphasized that although the increased risk had been detected in one long-term cancer-prevention trial, a second trial had indicated no increased risk. Nonetheless, concerns about this agent and all COX-2 inhibitors abound.

The National Cancer Institute had conducted the studies for Pfizer. In one trial, patients taking 400 to 800 mg daily were found to have a risk of experiencing major heart problems that was 2.5 times greater than that for people who were not taking the drug. The other cancer study found no increased heart risk with 400 mg/day.

Pfizer said that it was taking immediate steps to communicate the new information to regulators, physicians, and patients.

The National Cancer Institute suspended the first trial in which some patients were shown to have an increased risk of heart disease.

Pfizer said that it immediately shared the study results with the FDA and that it would work with FDA to sponsor a major clinical study to further assess the drug’s safety in osteoarthritis patients at high risk for cardiovascular disease.

The FDA plans to meet in February to re-examine all COX-2 drugs.

(Sources: Associated Press and The New York Times, December 17, 2004.)

**Warning Label for Valdecoxib**

The FDA said that it would require a new warning label for valdecoxib (Bextra®, Pfizer), another COX-2 inhibitor, because of potential heart problems associated with its use in people who had recently had heart bypass surgery.

Results from a study of more than 1,500 patients who had just had cardiac surgery show that patients treated with valdecoxib for pain were more likely to have heart attacks, strokes, and blood clots in the legs and the lungs, than patients who did not receive this agent.
Heart Risk for Naproxen Too? NIH Halts Study

Taking naproxen (e.g., Aleve®, Bayer AG), a pain reliever that is sold over the counter and by prescription, was found to increase the risk of strokes and heart attacks by 50% in a study by the National Institutes of Health (NIH). The drug has been on the market since 1976.

Researchers uncovered the problem during a review of data from an ongoing NIH study. That study was designed to determine whether nonsteroidal anti-inflammatory drugs (NSAIDs) could delay the onset of Alzheimer’s disease. The federal government announced that it was suspending the study as a precautionary measure.

Doctors urged consumers not to overreact to the potential heart risks.

Another recent study found a slightly increased risk of serious heart problems with naproxen or similar painkillers. But before these two studies, naproxen was thought to have no effect on the heart or to protect against heart attacks, although not as well as aspirin. The subjects had used naproxen daily for up to three years, far longer than is typical.

The FDA said it was reviewing the risks and had not ruled out restricting the drugs or taking them off the market. The FDA recommended that all patients taking naproxen without a prescription limit their use to no more than 440 mg/day (or 220 mg twice a day) for 10 days unless they consult their doctor. Bayer AG said that it agreed with the warning and believes the drug is safe at that dosage.

Some physicians have recommended that concerned patients switch to acetaminophen, aspirin, or ibuprofen.

The news challenges assumptions about heart protection because naproxen belongs to a drug class valued for its ability to prevent dangerous blood clots by thinning the blood. One doctor stated that biochemically and physiologically, it did not seem possible that the drug should cause heart attacks or strokes.

Doctors said they do not know how naproxen might hurt the heart. In other studies, patients taking naproxen experienced a 12% to 14% reduction in heart attacks, on average. However, another large study did find an 18% increased risk of heart problems with naproxen and a 33% increase with indomethacin, a similar but less commonly used drug.

In at least two studies, acetaminophen, which does not harm the stomach, is not as effective for arthritis as the COX-2 inhibitors or the over-the-counter NSAIDs.

Researchers said some of the hazards may not have come to light previously because they are relatively rare. The newer studies have been large and lengthy and have compared the drugs with placebos. Some earlier trials that compared the drugs to one another might have masked the problems.

The leader of the Alzheimer’s disease study said that the 70 heart attacks and strokes that occurred in the 2,400 patients was “not an alarming number” for a population over 70 years of age.

Some physicians thought that the trial’s duration might be a factor in the appearance of heart risks. The long-term effects of naproxen need to be studied.


Allergy Skin Testing Tray

Greer Labs has introduced the Skin-testor Omni™ allergy tray to test patients for allergen sensitivity. The tray can hold four Omni™ devices and up to 40 allergenic extracts. It fits securely over each well to protect the extract from spilling and to prevent contamination. Made of a sturdy synthetic clear plastic, the tray is 4 inches wide by 11 inches long. It can be stacked on top of another tray to save storage space.

(Source: Greer, November 30, 2004.)

NEW MEDICAL DEVICES

Marvin M. Goldenberg, PhD, RPh, MS
Name: QuantiFERON®-TB Gold Assay
Supplier: Cellestis International,
Valencia, CA
Approval Date: December 3, 2004
Use Classification: This blood test detects immune responses to proteins associated with tuberculosis (TB).
Description: Individuals primed in continued on page 26
Captique™ Injectable Gel

**Manufacturers:** Inamed/Genzyme

**Approval Date:** December 2, 2004

**Use Classification:** This gel is indicated for the temporary correction of moderate-to-severe facial wrinkles.

**Description:** Captique™ is a hyaluronic acid product in the dermal filler marketplace in the U.S. In 1996, this non-animal stabilized hyaluronic acid, created from fermentation and filtration, yielded a more purified hyaluronic acid and was formulated into a gel for use in Europe. This gel reduces the possibility of impurities and thus the incidence of sensitivity and allergic reactions.

**Purpose:** This form of hyaluronic acid is a facial soft-tissue expander.

**Benefit:** The gel has a low tendency to initiate allergic responses when it is used to treat severe facial wrinkles. It is safe and effective.

**Sources:** www.pharmacyonesource.com; http://archfami.ama-assn.org.

**Name:** NT-proBNP Heart Failure Test

**Manufacturer:** Dade Behring, Deerfield IL

**Approval Date:** December 2, 2004

**Use Classification:** The Nterminal pro-brain natriuretic peptide (NT-proBNP) test assesses the severity of heart failure.

**Description:** The fully automated test is available for use on Dimension® instruments with the heterogeneous immunoassay module.

**Purpose:** In patients with suspected CHF, measurements of NT-proBNP are used to diagnose heart disease and to assess its severity.

**Benefit:** B-type natriuretic peptide (BNP) is secreted by the left ventricle when the heart is unable to pump blood efficiently. BNP dilates blood vessels and promotes sodium and water loss, reducing fluid load on the heart and improving cardiac performance. NT-proBNP is released at the same time as BNP. Elevated plasma NT-proBNP levels indicate the presence of heart failure and provide information about its severity: the higher the blood levels of NT-proBNP, the more serious the condition. NT-proBNP levels have been shown to be a diagnostic aid in identifying left ventricular dysfunction, allowing physicians to differentiate between heart failure and lung disorders that manifest similar symptoms.

**Sources:** www.pharmacyonesource.com; http://biz.yahoo.com.

**Recalled Device**

**Item:** Universal Cable Adaptor for LTV® Series Ventilator

**Recalling Firm:** Pulmonetic Systems, Inc., Minneapolis, MN

**Date:** November 19, 2004

**Use:** This series of ventilators is intended to provide continuous or intermittent breathing support for adults or children who need mechanical ventilation. The adaptors were designed as a permanent field correction to an earlier class I recall because of failure of the ventilator to switch properly to using the internal battery when the external power source was unstable or inadequate, resulting in a loss of ventilation. Approximately 1,129 adaptors have been distributed.

**Reason for Recall:** The adaptor sometimes prevents the ventilator from being powered up again if the ventilator’s internal battery is depleted, or it may not be securely attached to the pigtail connector on the ventilator.

**Source:** www.fda.gov/cdrh/recalls.